Puget Sound Blood Center

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Subject: Comments on Draft Guidance for Industry—Biological Product Deviation Reporting for Blood and Plasma Establishments

To Whom It May Concern:

To effectively comment on the content of the draft guidance it is important to examine the impetus for the regulation. As described in the Federal Register, Docket No. 97N-0242, the stated purpose of the revision was to establish a timely reporting period for errors and accidents as well as to require unlicensed establishments to report. The FDA also sought to narrow the scope of reporting requirements to those that were necessary to protect public health while relieving some of the reporting burden. To this end, it is imperative that reports be timely, required, and truly relevant to the protection of public health.

The guidance document is appropriately succinct in specifying a 45-day reporting period and represents a consistent definition of who must report. However, the examples of reportable events by system represent more of a laundry list of possible errors rather than guidance showing CBER's thinking on what types of deviations are pertinent to the protection of public health. CBER's draft guidance does not enhance or boost the regulation with logic, rationale or evaluation systems to aid blood establishments in this regard. This is despite the fact that the draft guidance correctly requires the development of procedures to assess events and cautions that "(the SOP) should not consist of a list of examples of reportable and non-reportable events alone." Decisions on what to report should be defended by a basis in thinking rather than an arbitrary list of examples. Additionally, the numerous examples provided requiring multiple reports from the transfusion service, blood center and contractor greatly expand rather than relieve reporting burdens.

In most of the cases where reports are being advised, the likelihood of actual adverse effect is virtually nil. The FDA guidance must establish a clear reporting threshold, not sundry examples hoping that blood establishments and transfusion services can effectively reverse-engineer the fractured logic behind the list. Throughout the document, CBER defines certain issues as reportable if the violation has the "potential for" or "may have" detrimental effect on safety, purity, or potency. Yet, the draft guidance asserts that some items are NOT reportable due to the fact that a hazardous outcome is "unlikely". It can't be both ways.

Given the expansive list of deviations to be reported, the danger exists for CBER to be inundated with data of little consequence. Changes in donor suitability promulgated by the Agency are irrelevant to identifying public health threats. For example, new vCJD/CJD criteria are purely theoretical and have only the most remote potential for introducing hazard. Reports, if required, may affect donations long since transfused for which no product exists or only products sent for further manufacture, which are deemed acceptable. Reporting such cases jeopardizes CBER's ability to detect truly relevant trends.

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Similarly, reporting donor seroconversions lacks consequence. For most viral markers, recipient tracing is not even indicated. To initiate a report to the FDA because safety, purity or potency may be affected contradicts the rationale behind existing guidance in this area. Hepatitis B core and HTLV-I/II both merit a positive test on two separate occasions before the donor is deferred. To initiate a BPD without even deferring the donor is unreasonable.

Simply because something should not have happened does not mean that safety, purity, or potency was compromised. Shipment of pooled platelets rather than apheresis platelets does not mean that the product was inherently unsafe, impure or lacking in efficacy. Delays introduced in product delivery due to mix-ups at the hospital or transfusion service do not mean that the product has been compromised. Nor do labeling errors involving a missing platelet count, donor number, or weight (when were these even required?) introduce a potential harm to the patient. Failure to perform a QC procedure is not causal in a deviant product. Other failures would have been necessary to yield an unsafe, impure, or ineffective blood component.

It is our recommendation that the guidance be differently structured, perhaps using fault tree analysis. In this way, the FDA would establish those failure modes (outcomes/potential outcomes) that would require a report rather than all of the ways in which an establishment might inflict or suffer such a consequence. These outcomes should be defined in a manner where the hazard is clear and imminent, not suspect or surmised. The focus needs to be directed at the nature of the risk rather than the myriad ways that the risk can be introduced. This approach would also prevent the circumstance where, depending on the policies of the institution, some things may be reported by one facility, but not by the other.

Examples, including but not limited to:

Hazard	Effect	Threshold	Is a BPD Report Indicated?
Distribution of a unit at increased risk for communicable disease transmission	Not safe	o Was the risk imminent and without downstream detection measures? o Was the risk remote (i.e., a seroconversion) and the previously distributed units tested negative with a licensed test?	Yes No
Use of a donor found unsuitable for donation	Not safe	o Was the donor determined to be infectious or at increased risk of infection? o Was the donor theoretically infectious without established evidence of transfusion transmission? o Was the risk to the donor only with no adverse effects known to the intended recipient?	Yes No No
Adverse patient outcome	Not pure	o Was the patient adverse effect related to a failure of process control in the manufacture of the blood component? o Was the patient adverse effect due to unique donor properties? o Was the adverse effect due to the underlying disease state or condition of the patient?	Yes Yes No
Misrepresentation of product Etc…	Not potent	o Was the product labeled in a manner that misrepresented properties of the product? o Was an incompatible product distributed to the transfusionist? o Was the wrong product ordered? o Was the wrong product distributed to the transfusionist? o Was the product's delivery delayed?	Yes Yes No No No

The other "stuff" (e.g., hemolyzed or clotted segments, missing social security numbers, wrong products, SOPs not followed, underweight units, collection status, missing information later found to be acceptable, etc.) should be stripped from the guidance. Simply because an event happened, was reported, entered into a database, and acknowledged, does not serve as the basis for a reporting threshold. It is imperative that the FDA establishes a more robust criterion for differentiating that which is reportable from that which is not. Rather than adding to the list, simplifying and characterizing risk is indicated.

Thank you for the opportunity to comment on the draft guidance. We support the Agency's interest in protecting public health. We continue looking forward to meaningful output from the Biological Product Deviation system beyond quarterly reports. Should you have any questions, please contact Linda Barnes, (206) 292-4688.

Sincerely,

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